

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Gary L. Nelsestuen  
Title : MODIFIED VITAMIN K-DEPENDENT POLYPEPTIDES

Commissioner for Patents  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the Specification

Please replace the paragraph beginning at page 1, line 4 with the following rewritten paragraph:

--This application is a continuation of U.S. Serial No. 09/302,239, filed April 29, 1999, which is a continuation-in-part of U.S. Serial No. 08/955,636, filed on October 23, 1997, now issued as U.S. Patent No. 6,017,882.--

In the Claims

Please cancel claims 1-22.

Please add the following new claims.

--23. A protein C or activated protein C polypeptide comprising a modified GLA domain, said modified GLA domain comprising at least one amino acid substitution selected from residues 11, 12, 29, 33 and 34.

CERTIFICATE OF MAILING BY EXPRESS MAIL

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March 12, 2001

Date of Deposit

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Vince Defante

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24. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 11.

25. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 12.

26. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 29.

27. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 33.

28. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 34.

29. A protein C or activated protein C polypeptide comprising a modified GLA domain, said modified GLA domain comprising three amino acid substitutions at positions selected from the group consisting of residues 11, 12, 29, 33 and 34.

30. The protein C or activated protein C polypeptide of claim 29, wherein said three amino acid substitutions are at residues 12, 33 and 34.

31. The protein C or activated protein C polypeptide of claim 30, wherein residue 33 is glutamic acid.

32. The protein C or activated protein C polypeptide of claim 30, wherein residue 34 is aspartic acid.

33. The protein C or activated protein C polypeptide of claim 30, wherein residue 33 is glutamic acid and residue 34 is aspartic acid.

34. The protein C or activated protein C polypeptide of claim 29, wherein residue 11 is glutamine.
35. A pharmaceutical composition comprising said protein C or activated protein C polypeptide of any one of claims 23-34 and a pharmaceutically acceptable carrier.
36. The composition of claim 35 for use in treating thrombosis in a mammal.
37. The composition of claim 35 for use in decreasing clot formation in a mammal.
38. The composition of claim 36, wherein said composition is formulated for parenteral administration to a human patient.
39. The composition of claim 37, wherein said composition is formulated for parenteral administration to a human patient.
40. An isolated nucleic acid, said nucleic acid comprising a nucleic acid sequence encoding said protein C or activated protein C polypeptide of claim 23 or claim 29.
41. A method of producing the protein C or activated protein C polypeptide of any one of claims 23-34, said method comprising expressing an isolated nucleic acid encoding said protein C or activated protein C polypeptide in a mammalian host cell.
42. The method of claim 40, wherein said mammalian host cell is an adenovirus-transfected human kidney 293 cell.--

REMARKS

Applicants have canceled claims 1-22 and submitted new claims 23-41. Support for these claims can be found throughout the specification, including at page 9, lines 14-20, page 10, line 10 through page 11, line 14, page 13, lines 26-27, page 15, lines 22-25, page 17, lines 18-20, and at page 33, lines 25-28. No new matter has been introduced.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made."

Applicant submits that all of the claims are now in condition for examination, which action is requested.

A check is enclosed for payment of excess claim fees.

Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 3/12/01

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**Version with markings to show changes made**

**In the specification:**

Paragraph beginning at page 1, line 4 has been amended as follows:

This application is a continuation of U.S. Serial No. 09/302,239, filed April 29, 1999, which is a continuation-in-part of U.S. Serial No. 08/955,636, filed on October 23, 1997, now issued as U.S. Patent No. 6,017,882.